The Value of C-Reactive Protein Estimation as Screening Test for Ischemic Heart Diseases.

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Abstract

Background: C- reactive protein synthesized by hepatocytes in response to proinflammatory cytokines, CRP has axial rule in many aspects of athrogenesis.

Objectives: The study aimed evaluated the rule and estimating serum "C-reactive protein" level in ischemic heart diseases and relation with lipid profile levels, hypertension and inflammation.

Materials and Methods: Seventy-five adult male and female were enrolled in this study, divided into the three groups, 25 each (CCU admitted patients, outpatients clinic and healthy controls). All their blood samples were checked up for lipid profile. "Erythrocyte sedimentation rate" (ESR) estimation and high sensitivity "C – reactive protein" (hs – CRP).

Results: Study showed (significant, weakly, non – significant, correlation between high level of "hs – CRP' with lipid profile level to hypertension, inflammation and ischemic heart diseases.

Conclusion: There are relation with high level of (hs-CRP) to inflammation, infection, hypertension which in the end lead to a heart disease.

High level of " hs-CRP" is expected to be an indicative to abnormal lipid profile which might contribute to increase the risk of atherosclerosis.

Keywords: C-reactive protein , Ischemic heart diseases ,ESR .

Introduction:

C-reactive protein" is a molecule that was first isolated from patients with pneumococcal pneumonia in 1930[(1)] . It was so termed because of its binding with the" C- polysaccharide" of the pneumococcus .It is often called an "acute – phase protein" [(2)] .Now a days a high – sensitivity C-reactive protein test , usually designated as (hs – CRP) measures low levels of(CRP) using laser nephelometry [(2)] Many studies suggest that an elevated "hs – CRP" is predict of "coronary heart disease" and cardiovascular risk ,CRP is a "non – a specific acute phase" reactant to both "infective and non – infective" and inflammation ,(CRP) values less than 10mg/L, such CRP measures is called "hs _CRP". The range of "hs_ CRP" in serum is "3 – 10 mg/L" [(3)].Atherosclerosis: It Is a major cause of "morbidity and mortality" the worldwide , which is increasing dramatically with time. It includes (coronary heart disease), atherosclerosis, (vascular disease) and (cerebrovascular disease.) The coronary heart disease: it is due to blockage in any one of the coronary arteries leading to in sufficient blood flow and oxygen supply to the heart. **Lipids**: The (organic compound) of lipids have many similarities. They are almost always (greasy, fatty, oily, or waxy). "In general healthy lipid levels" it help to maintain a "healthy heart" and lower [(4)]
therisk of heart attack or stroke. (5)Lipid profile typically includes - Total cholesterol (TC),High – density Lipoprotein cholesterol (HDL-C) .- Low – density lipoprotein cholesterol (LDL-C) ,Triglycerides (TG)and very low – density lipoproteins (VLDL-C).[(5)]."Erythrocytes sedimentation rate" (ESR):High ESR ,any inflammatory disorder ex. infection, rheumatoid, tuberculosis, myocardial infraction early response , anemia, polymyalgia rheumatic, temporal arteritis[(6)].Combined use of ESR and CRP is useful in assessing the severity of acute pelvic inflammatory disease .Both (ESR &CRP) are biomarkers for inflammation, ESR & CRP should be interpreted differently. Due to this "basic physiologic difference", CRP is a more sensitive and accurate reflection of the acute phase of inflammation than ESR. [(6)]Aim

1 – Evaluate the rule of CRP level as screening test for schemic heart diseases.

2 – Estimating serum CRP level in ischemic heart diseases and relation with lipid profile levels, hypertension and inflammation.

3 – Highlight the effect of different risk factors on CRP level.

Patients and Methods:

The study started from 25 September 2016 till end of December 2016. An information form was prepared and designed according to questionnaire which cover all information. Samples were collected from patients admitted to

Al – Yarmouk Teaching Hospital in Baghdad. Sample from apparent healthy persons which used as control group were collected from staff of

Al – Mustansiriya University / College of Medicine.

Sample Collection: About 5 – 7 ml of venous blood was drowned from redial vein from each one. Each samples divided into two tubes one had (EDTA) tube and other in plain tube to get a serum then serum divide in to two tubes one to lipid profile analysis and other serum dispensed in to micro pipettes (Eppendrof) which kept at 30° – 40° c till use to measure (hs CRP) in AL-Mustansiriyah University National Center Of Hematology.

Seventy Five (75) samples were collected from three groups which enrolled into the study:-
A-CCU patients group a total 25 samples were collected from CCU department whose ages from (34-65) years.
B-Outpatients group a total 25 samples were collected from outpatient clinic whose ages from (40-65) years.
C- Apparently healthy persons as control group 25 samples were collected from Al-Mustansiriyah University / College of Medicine whose ages from (33-65).
Study Groups: Seventy Five (75) samples were collected from three groups which enrolled into the study :-
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Methods: 1 – "High sensitivity C – reactive protein" (hs – CRP) test was done by using ichroma device from (Boditech med. incorporated) company in Al – Mustansiriyah University / National Center of Hematology. The test uses a sandwich immune detection method ; the detector antibody in buffer binds to antigen in samples.
2 – Lipid profile analysis and Erythrocyte sedimentation rate (ESR) conducted in Biochemistry Lab. And Hematology lab. In Laboratory department in Al – Yarmouk Teaching Hospital.

Lipid profile analysis conducted by Abbott device (ARChitech) Alkaloidal Company, Abbott Laboratories Medical device.
1 – Total Cholesterol (TC) : This test measures all of the cholesterol in all the lipoprotein particles
2 – Triglycerides (TG) : measures all the triglycerides in all lipoprotein particles ,
3 – High – density Lipoprotein (HDL _C) : measures in all lipoprotein HDL particles , often called "bad good Cholesterol
4 – Low – density Lipoprotein (LDL _C) : measures the Cholesterol in LDL particles, often called "bad Cholesterol
5 – very low – density Lipoprotein (VLDL): Calculated from triglycerides / this formula is based on the typical composition of VLDL particles.
Statistical Analysis: Data were expressed as mean ±SEM, the comparison between groups was by using ANOVA, $P < 0.05$ was considered as statistically significant. Independent t-test was used to compare between any two groups. Correlation test between variables considered $r >\pm 0.3$ as statistically significant (7).
Results:- Seventy five individual were enrolled in the study and divided into three groups, 25 each, CCU admitted patients, Outpatient clinic and healthy controls.
Table (1) : In this table sex distribution among the studied groups showed no significance between females and males , also showed the distribution of age (years) and BMI(kg /m²) among the studied groups was reported high significant to age only in outpatient while no significance in both CCU patients and healthy control groups whereas no significance between all groups to (BMI/m²)

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Table 1: Sex, Age (years) & BMI (kg/m²) distribution among the studied groups.

				Chi-Square P-value
	CCU	**Outpatient**	**Healthy**	
Females	14 (56%)	9 (36%)	11 (44%)	0.36
Males	11 (44%)	16 (64%)	14 (56%)	
	Group (Mean±SEM)			
	CCU	Outpatient	Healthy	
Age (years)	50.72±1.46	65±1.45**	44.72±2.32	0.001
BMI (KG/m^2)	29.06±0.82	37.11±0.8	26.86±0.81	0.162

Table 2: Lipid profile values (mg/dl), ESR (mm/hr) & CRP levels among the studied groups (Data represent Mean±SEM, *= statisical siginifcance of P-value <0.05, **= high statistical significance of P-value<0.01)

Lipid profile (mg/dl) ESR	**Group (Mean±SEM)**			**P-value**
	CCU	**Outpatient**	**Healthy**	
S. Cholesterol	196.04±12.54	220.6±17.05**	158.12±4.96	0.003
S. Triglyceride	208.88±17.01**	198.32±21.72**	117.52±5.13	0.000
S. HDL	36.4±1.87	38.6±1.65	36.15±1.35	0.510
S. VLDL	42.08±3.38*	39.84±4.37*	23.2±1.06	0.043
S. LDL	123.56±12.44	139.76±17.12**	95.16±4.23	0.000
ESR (mm/hr)	22.48±2.35**	19.56±2.01	13.28±1.1	0.003
CRP	8.53±0.56**	7.72±0.64**	1.99±0.27	0.000

Table 3: Categorization of lipid values profile

Lipid profile (mg/dl)	Desirable	Borderline	High risk
S. Cholesterol	<200	200-239	240
Triglycerides	<150	150-199	200-499
LDL Cholesterol	60-130	130-159	160-189
VLDL	2-30	-	>30
HDL Cholesterol	60	35-45	<35

Table 4: CRP values according to lipid profile categories (Data represent mean SEM, *= statistical significance of P-value <0.05, **= highly statistical significance of P- value <0.01)

Lipid profile	Category	CRP (Mean±SEM)	P-value
S. Cholesterol	Desirable	5.43±0.53	0.029
	Borderline	7.31±1.06	
	High risk	8.79±0.67*	
Triglycerides	Desirable	3.8±0.53	0.000
	Borderline	8.01±0.93**	
	High risk	9.04±0.48**	
LDL	Desirable	5.18±.054	0.021
	Borderline	7.72±1.05	
	High risk	8.64±0.74*	
VLDL	Desirable	5.18±0.54	0.000
	High risk	8.64±0.74**	
HDL cholesterol	Desirable	7.77±1.14	0.246
	Borderline	5.51±0.6	
	High risk	6.3±0.81	

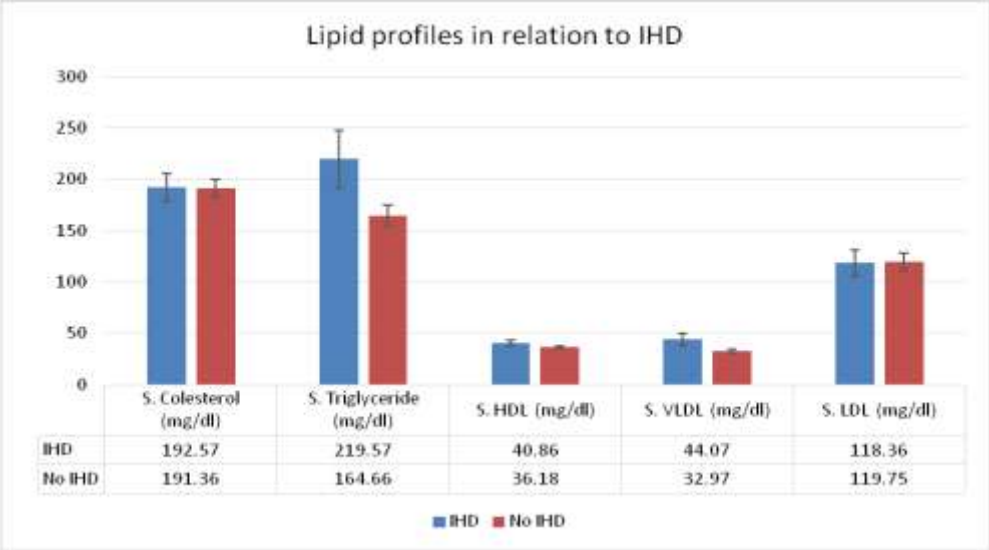

Figure 1: Lipid profile values in patients with IHD (Data represent Mean, error bars represent SEM, *= statistical significance of P-value <0.05)

Lipid profile values in patient with IHD this figure showed significant relation between S.TG and VLDL and in IHD when comparative with no IHD. And no significance in S.TC , HDL and S.LDL in both IHD & no IHD

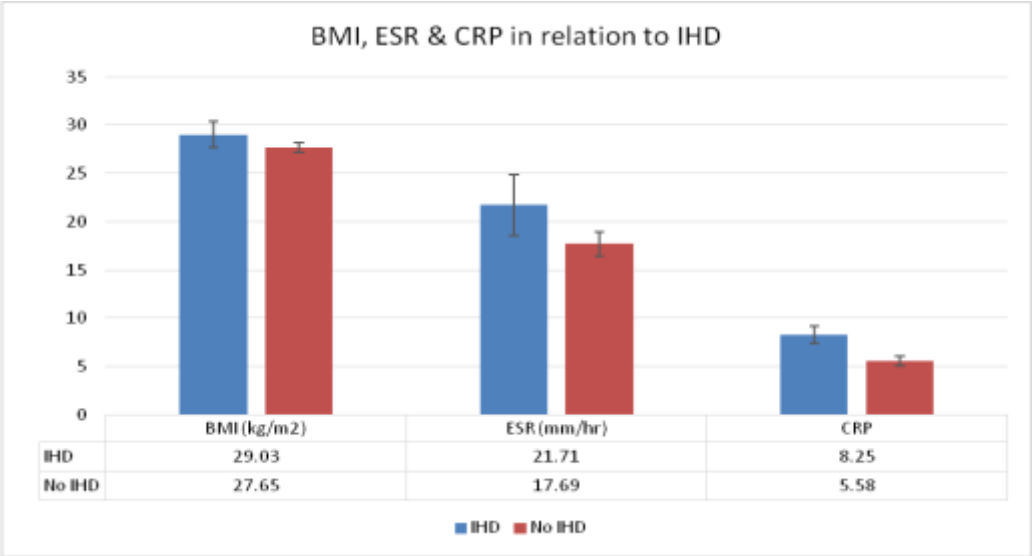

Figure2: BMI (Kg/m2), ESR (mm/hr) & CRP values in patients with IHD (Data represent Mean, error bars represent SEM, *= statistical significance of P-value <0.05)

This figure show. BMI, ESR, CRP in relation to IHD, appear significant relation between CRP & IHD when compare with no IHD and no significance in BMI, ESR in both IHD & no IHD.

Discussion: C-reactive protein, or CRP is produced whenever something is starting become inflamed the risk of having heart diseases, heart attack, stroke and peripheral arteries insufficiency is greater whenever the arteries are inflamed. Seventy five individuals were enrolled in the study and refer to statistical studied groups. The results showed many relations and correlations between CRP levels and their lipid profile, age, sex, body mass index (BMI), hypertension and ischemic heart diseases.

Abnormal lipid profile plays a main role as risk factor to increase hypertension, so there is a relation between lipids and hypertension, aside from another factors which have role to increasing hypertension. In this study the abnormal lipid profile value differed significantly among three groups except for HDL value which were not significantly different (table 2.).Serum triglycerides (TG) and very "Low – density lipoprotein" (VLDL) had significantly greater values in both CCU patients and outpatients. Serum total cholesterol (TC) and Low – density lipoprotein (LDL) levels were significantly higher in outpatients only, (S.TC and S.TG) was had high significant in both CCU patient outpatient groups.

A ll CCU patient and outpatient groups were had hypertensive so there results explain the relationship between hypertension and dyslipidemia which are the main risk factor for "cardiovascular disease" (CVD) and this study agree with study by Kannel WB. (2000) (8). "High sensitivity of C - reactive protein" levels were "significantly higher" in patient who has high risk measurements of (TC), (TG), (LDL&VLDL).They were also "significantly higher" in patients with borderline (TG) levels,(hs - CRP) levels were not significantly different among the categories of HDL measurement so there was a moderate positive correlation of "hs - CRP" with (TG), with VLDL. There was no correlation between (CRP) and (HDL TC). This study agree with another study by (Elaine paffen, et al. 2006) (9).

When the interaction between lipid and (CRP) is different. It has been proposed that (CRP) could be the factor that binds "lipoprotein – deposition" and complement activation in atherosclerotic plaques. Linking of tissue–deposited (CRP) to enzymatically low LDL promote complement activation, which may be relevant to the expansion and headway of the "atherosclerotic harm". This proved by Trozewski j, et al. 1998 (10).

The relation of lipid profile to inflammation .This agree with study by MD KF, 2000 (11) that is improve and explain our results infections and inflammation included changes in lipid metabolism increase in both TG and VLDL, as well affecting the serum lipid levels, inflammation also adversely effected lipoprotein function in the body.

Relation of (ESR & CRP) to hypertension were Increase of "hs CRP" level in this study observed of hypertension patients, this raises may be subclinical inflammation or infection as indicated by (CRP) and may be one of the accidental mechanisms contribute to an increased for "myocardial infarction" (MI) in hypertensive patients and this agree with study which done by G. Schillaci 2003 (12). Dyslipidemia one of the power full warning of harm "cardiovascular disease". Source endothelial, the harm may raise systemic blood pressure, hypertension has persistent and strong relationship with risk of (CVD) events. And this is matches the study which by Oparils, et al 2003 (13).

The study showed significant relation between (ESR&CRP) and inflammation which is strongly accepted as trigger for atherosclerosis response for – injury hypothesis. This agree with study by Ridker PM. 2009(14) which explain the test to inflammatory hypothesis of atherosclerosis, without decreasing lipid is to directly haphazard patients to targeted anti – inflammatory treatment.

The study showed increased level of "hs – CRP" and dyslipidemia is observed among patients with hypertension, this correlation confirmed that(CRP) is indicative of high level of lipid profile and this agree with the study by Gupta R. 2004 (15) which increased of "hs –CRP" also is an inflammatory tick which can stimulation inflammatory alteration the endothelial and smooth muscles cells and is associated with evolution and headway of hypertension and atherosclerosis and this result conform with study which done by Van Der Meer, et al (2002) (16).

All tables (2,3,4) and figures (fig.1,2) reveal that there is a significant statistical correlation between the level of "hs-CRP" and the modifiable risk factors (Hypertension, Hyperlipidemia, inflammation) for Ischemic heart diseases (IHD) and there is a research suggesting that the use of "Anti – CRP antibody" can be used as preventive measure to reduce the risk of having "Ischemic heart diseases" in patient with variable degrees of atherosclerosis or coronary arteries in sufficiency , the study done by Kearny Pm.;(2005). (17) .Inflammation as evidence by CRP, may be one of the causative mechanisms share in an increased risk for myocardial infarction in hypertensive patient and this agree or matching with study by G.J Blake et al . (2003)

There is a significant difference in(ESR & CRP) levels between males and females and this result matching with study which done by Siemons L,et al , 2014 (19) which explained high levels or increases of levels in women than men.There was no significant relationship between body mass index (BMI) to hypertension which is not agree with study which done by. Droyvold WB, et al .2005 (20) which explained that significant positive relation among BMI and blood pressure (hypertension).

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